

modify the teachings of the prior art reference to achieve the presently claimed invention, and (ii) a reasonable expectation of success in making and using the modified procedure.

Tycko teaches an apparatus and method for measuring volume and hemoglobin concentration of individual red blood cells using the signals detected by a scattered light detector and a resistance pulse detector. The present invention claims a method and apparatus for a simultaneous determination of red blood cell properties including volume, hemoglobin content, normal/abnormal cell shape and maturity, plus determination of immature red blood cells (reticulocytes) and white blood cell differential analysis. These measurements are achieved through a pre-calibrated three-dimensional surface generated using five types of optical signals and using only one optical detection system.

Tycko only teaches the use of two variables for the determination of volume and hemoglobin concentration of red blood cells. It does not teach using the three features of the present invention, i.e. a forward angle scatter, a light loss scatter and a side angle scatter. This multi-angle light scatter analysis is needed for the more complex and more difficult differential analysis of abnormal red blood cells. Tycko's patent does not teach the simultaneous determination of red blood cell properties, normal/abnormal cell shape and maturity, and the determination of immature red blood cells (reticulocytes) and white blood cell differential analysis as in the present invention.

Altendorf teaches an optical analyzer for planar liquid sample flow cells comprising a polarized light source and at least two large angle scattered light photo-detectors (15° - 50° and 50° - 130°, Column 11, line 17)). The present invention does not use two large angle scattered light photo-detectors. In the present invention, all selected forward angles used for volume measurements are very small (0, 1-3 or 4.5-5.5) and only the side scatter has a large angle. Altendorf's optical analyzer does not permit the simultaneous determination of red blood cell properties including volume, hemoglobin content, normal/abnormal cell shape and maturity, plus determination of immature red blood cells (reticulocytes) and white blood cell differential analysis as the present invention does. Altendorf's optical analyzer permits only the separation of red blood cells from platelets by their size differences as shown in Figures 8 and 9 of the "157 patent".

Regarding claims 14 and 15, the present Office Action refers to Figure 3 of Tycko as indicative that scattering obtained from a range of angles (front, intermediate, and side) are used to obtain hemoglobin concentration and blood volume. Tycko does not teach using side angle scatter and does not teach measuring both, cell volume and cell hemoglobin concentration by light scatter signals. Tycko teaches measuring cell volume by resistant pulse size of each red blood cell passing through an impedance aperture. Figures 3a through 3d do not show 3 variables but only displays 3 different hemoglobin concentration (HC) curves between 0° and 25° forward angles to show which angular interval generates linearity for cell hemoglobin concentration. Figure 3 shows that at a wavelength of 0.6328  $\mu\text{m}$ , the only region for HC linearity is between 18° and 25°. All the other regions do not generate signals that are linear to HC.

The present invention claims the use of three scatter signals displayed in a three-dimensional grid surface, which permits white blood cell and red blood cell differential analysis using the same light source and same optical detection system (same flow cell, same optical detector and same pre-amplification board). These features are emphasized in parts (e) and (f) of claim 13.

Regarding claims 19 and 20, the present Office Action refers to the wavelength used in Tycko's patent (632 nm) as falling within the wavelength range of the present invention. The present invention uses the whole range of the visible spectrum because shorter visible wavelength light sources (for example 488 nm and 523 nm) permit the use of more sensitive nuclear stains for DNA and RNA that permit identification of, for example, immature red blood cells. Tycko's patent teaches measurement of volume and hemoglobin concentration of red blood cells only, therefore the scope of the wavelength needed in Tycko's patent is different from the scope of the wavelength needed in the present invention, which determines not only volume and hemoglobin concentration of red blood cells, but also normal/abnormal cell shape and maturity, immature red blood cells (reticulocytes) and white blood cell differential analysis.

Applicants respectfully submit that Tycko and Altendorf alone or in combination do not describe, teach, or suggest, in either patent alone or in combination, to modify the apparatus described in each of the referenced patent and to obtain the apparatus claimed

However, counting and differentiating white blood cells without lysing red blood cells in a sample presents the problem of counting one blood cell for every 100 to 500 red blood cells. In the present invention, red cells are lysed in the white cell channel keeping the sample dilution factor at the minimum to count enough cells in a short time (e.g. 8 seconds) in order to accommodate the need in the general clinical setting. Simultaneous white and red blood cell analysis is done using the same time-sharing flow cell, the same optical detector and the same pre-amp board as described in parts (e) and (f) of Claim 13 of the present invention. The optical detector originally designed for white blood cell differential analysis is modified to have multiple discrete regions, corresponding to predefined angular intervals for both red and white blood cell analysis. The system pre-amp board is also modified to selectively isolate desired angular intervals for white blood cell and red blood cell differential analysis, respectively.

Tycko, Altendorf and Kirchanski combined fail to teach the simultaneous determination of RBC characteristics and the WBC differential analysis. Therefore, neither Tycko, Altendorf nor Kirchanski alone or in combination teach or suggest, as the instant invention does, a method and apparatus for the simultaneous determination of red blood cell properties including volume, hemoglobin content, normal/abnormal cell shape and maturity, plus determination of immature red blood cells (reticulocytes) and white blood cell differential analysis.

In view of the above discussion, Applicants respectfully request that the rejection of claims 17 and 18 be reconsidered and withdrawn.

**CONCLUSION**

Applicants respectfully request the issuance of a Notice of Allowance. If the Examiner notes any further matters that the Examiner believes to be expedited by a telephone interview, the Examiner is requested to contact the undersigned.



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Respectfully submitted,  
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A handwritten signature in cursive script, appearing to read "Regina M. Anderson", written over a horizontal line.

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